selected from the group consisting of vaccines and plasma derivatives.

REMARKS

New claims 18 and 19 have been added. An equal number of claims have been cancelled. In addition, new claims 18 and 19 are dependent on claim 1 and raise no new issues for consideration or in any way add new matter to the specification. Support for claims 18 and 19 may be found on page 9, first full paragraph, of the specification. As such, entry and consideration thereof are respectfully requested.

Objections to the claims

Claim 15 has been objected to for the grammatically incorrect recitation of "viruses." Claim 15 has been amended to correct this grammatical error. Withdrawal of the objection is, therefore respectfully requested.

Rejections under 35 U.S.C. §112, first paragraph

The Examiner maintains the rejection of claims 1-10 and newly rejects claims 13-16 under 35 U.S.C. §112, first paragraph for lack of enablement. More specifically, the Examiner asserts that the specification is not enabled for inactivating viruses in cell cultures by contacting the compositions with cyclic lipopeptides in concentrations greater than 70μM. The Examiner relies on a teaching of Vollenbroich et al. that the cyclic lipopeptide, surfactin, is lethal at concentrations greater than 70 μM. Claim 1 has been amended to be drawn to non-cell culture biological products. As such, the present invention as encompassed by claim 1 and dependent claims thereon is no longer drawn to

inactivating viruses in cell cultures with concentrations of cyclic lipopeptides greater than 70μM. Withdrawal of the rejection is, therefore, respectfully requested.

Rejections under 35 U.S.C.§112, second paragraph

The Examiner maintains the rejection of claim 1 under 35 U.S.C. §112, second paragraph as being unclear with regard to the distinction between "cell cultures" and "biological products." The Examiner asserts that "biological products" encompass "cell cultures." Claim 1 has been amended to more clearly recite "non-cell culture biological products." As such, withdrawal of the rejection is respectfully requested.

Claim 10 has been rejected with the assertion that the metes and bounds of "herpes viruses" and "immunodeficiency viruses" cannot be determined. Applicants traverse this rejection and withdrawal thereof is respectfully requested. The terms "herpes viruses" and "immunodeficiency viruses" are well known terms in the field of the invention. Attached hereto as Exhibit A are excerpts from "Fields et al., Virology, 3rd ed., Philadelphia-NY (1996), which is a standard text-book in the field of virology. As detailed on pages 45 and 46 from the chapter on virus taxonomy, "herpes viruses" are a well-characterized family of viruses. Similarly, as detailed on pages 40 and 41 "immunodeficiency viruses" are known to encompass, for example, human immunodeficiency viruses 1 and 2, in humans; feline immunodeficiency viruses; bovine immunodeficiency viruses; and simian immunodeficiency viruses, which include, for example, mandrill virus, chimpanzee virus, and rhesus virus). Thus, the terms "immundeficiency virus" and "herpes virus" are well-known terms of art whose meaning

would be readily apparent to one practicing the invention. Withdrawal of the rejection is therefore respectfully requested.

The Examiner maintains the rejection of claim 12 for insufficient antecedent basis, noting that the response of September 9, 2000 failed to cancel the claim. Applicants apologize for this oversight. Claim 12 has been cancelled herein, thus addressing this issue.

Rejections under 35 U.S.C. §103

The Examiner maintains the rejection of claims 1, 3, 4-7, 9 and 10 and newly rejects claims 14-17 under 35 U.S.C. §103 as being obvious over Itokawa et al. The Examiner indicates that the arguments of September 9, 2000 are insufficient because the claims do not recite a degree of viral inactivation that must be achieved. Claim 1, and all dependent claims thereon, have been amended to recite that the degree of viral activation achieved using the claimed method is an inactivation factor $> 10^4$. This amendment is supported by page 8, paragraph 3 of the specification. Itokawa et al. disclose only a moderate amount of anti-HIV-1 activity and there is no disclosure in Itokawa et al. of inactivation by a factor of $> 10^4$. An inactivation factor of $> 10^4$ is considered to be indicative of a strong level of inactivation. For example, as demonstrated in Example 5 of the specification, after 60 minutes no infectious particles could be found.

The Examiner asserts that the teaching by Itokawa et al. of a moderate amount of inactivation points directly to the use of cyclic peptides. However, this assertion is hindsight reconstruction of the invention. At the time of Itokawa et al. thousands of

compounds had been identified which had "moderate" viral inactivation activity at least to the degree, or even somewhat better than that, of Itokawa et al. No reason has been presented by the Examiner to select the compounds of Itokawa et al. over the compounds of any other reference. There is no suggestion in Itokawa et al. that one would be able to achieve the degree of activation in the short time recited with the present invention. As such, the present invention is neither taught nor suggested by Itokawa et al. and withdrawal of the rejection is respectfully requested.

The Examiner further maintains the rejection claims 1, 3, 9 and 10 under 35 U.S.C. §103 as being obvious over Naruse et al. In response to the arguments of September 9, 2000, the Examiner asserts that Naruse et al. teaches an incubation of 72 hours to allow sufficient time for the formation of CPE as an indicator of HSV viability/inactivation not as the length of time required for virus inactivation. The Examiner further notes that the argument that the pumilacidins are different than surfactins is insufficient because the claims are not limited to surfactins. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

A virus is a non-cellular entity that can only reproduce within a host cell. A characteristic of viruses is that the replication cycle (making copies of DNA or RNA) take place inside the host cell. Viruses consist of nucleic acid covered by protein. The virus uses the synthesis capabilities of the host cell to make progeny virus particles.

Viruses may be inactivated in two ways, a) indirectly or b) directly. An example of indirect viral inactivation is the treatment of virus-infected cells with an agent such as AZT (3'-azido-3'-deoxythymidine), which is a classical AIDS drug. AZT works by

preventing insertion of the genetic material (RNA) of human immunodeficiency virus into the host genetic material (DNA), thus blocking viral replication. With indirect viral inactivation, the agent (AZT) stops the virus from multiplying, but does not actually "kill" the virus.

In contrast, with direct viral inactivation, the virus actually killed. The agent attacks the viral membrane, for example, and kills the virus by disintegrating it. The present method is a direct method of inactivating viruses.

Naruse et al., on the other hand, disclose a method of indirect viral inactivation because with the method of Naruse et al. the host cell-dependent replication of the viral genetic material is being targeted and affected. With the method of Naruse et al. viral growth and multiplication is being inhibited. Naruse indicate on pages 274-275, regarding "Antiviral Activity,"

> Aliquots (50 μl each) of medium containing various concentrations of the test compounds were poured into wells of a 96-well microplate and 200 μl of the cell suspension...was added. To each well...virus was added.

With the method of Naruse et al. in the first step the test compound (e.g. pumilacidin) was added to the cells. In the second step virus was added to the test compound-treated cells. Naruse et al. further state on page 275, paragraph 1, that "Acyclovir was used as the reference compound in the assay." Acyclovir is an antiviral compound that is used to treat herpes virus through the indirect activation of the virus, by inhibiting synthesis of viral genetic material in host cells, similarly to the action of AZT with retroviruses. Acyclovir acts by inhibiting reverse transcriptase in the host cell. Thus, the method of Naruse et al. is an indirect method of viral inactivation that does not work by "killing" the viruses.

As noted above, the present method is directed to a method of directly inactivating viruses by killing them. The present method attacks the virus, completely independently of the host cell and the replication cycle of the virus in the host cell. There is no suggestion in Naruse et al. of a method of directly inactivating viruses. As such, the present invention is not obvious over Naruse et al. and withdrawal of the rejection is respectfully requested.

The Examiner maintains the rejection of claim 2 under 35 U.SC. §103 as being obvious over Itokawa et al. or Naruse et al. combined with Horowitz et al. and the rejection of claims 8, 11 and 12 has being obvious over Itokawa et al. or Naruse et al. combined with Vater et al. Inasmuch as the invention encompassed by claim 1 is not obvious over Itokawa et al. or Naruse et al. dependent claims 2, 8 and 11 are similarly not obvious when the Itokawa et al. or Naruse are combined with either Horowitz et al. or Vater et al. Withdrawal of the rejections is, therefore respectfully requested.

Should the Examiner have any questions regarding the present application, she is requested to please contact MaryAnne Armstrong, PhD (Reg. No. 40,069) in the Washington DC area at (703) 205-8000.

Pursuant to 37 C.F.R. §§1.17 and 1.136(a), Applicants respectfully petition for a one (1) month extension of time filing a response in connection with the present application and the required fee of $110.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §1.16 or under 37 C.F.R. §1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By 

JOE MCKINNEY MUNCY
Reg. No. 32,334

MARYANNE ARMSTRONG
Reg. No. 40,069

P.O. Box 747
Falls Church, VA 22040-0747
(703) 205-8000

KM/MAA/csp